# **The NICHD Connection**

## December 2020

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Eunice Kennedy Shriver National Institute of Child Health and Human Development

Then and Now: Studying Essential Proteins of the Nuclear Pore Complex

By Paul Elizalde

Researchers can study the role of specific proteins by mutating or getting rid of the protein and seeing what happens to the cell. However, some proteins are essential for cellular growth and survival, so how do you study a protein when removing it kills the cell?

Dr. Vasilisa Aksenova encountered just this problem while studying nuclear pore complex (NPC) proteins, known as nucleoporins, which are needed to move molecules, such as RNA, between the nucleus and cytoplasm.

"RNA export is a highly regulated point for all human gene expression," Dr. Aksenova explained. "Understanding it has broad implications for understanding disease mechanisms and designing targeted therapeutics." Her research teases out the role of individual nucleoporins and simultaneously supports a way forward in studying essential proteins.

Dr. Aksenova received her doctorate in cell biology from the Russian Academy of Science. When she wanted to focus on the cell biology

of the nucleus, Dr. Mary Dasso's lab at the NICHD was her first choice. She joined as a visiting postdoctoral fellow interested in nucleoporin function in mitosis. Continuing her work in the same lab, she says that her interest has broadened beyond mitosis. Her recent publication in *Nature Communications* focuses on the role of the basket nucleoporin, TPR, in mRNA export.<sup>1</sup>



Vasilisa Aksenova, PhD

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# Then and Now: Studying Essential Proteins of the Nuclear Pore Complex

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Based on biology's "central dogma," there are three levels that you can target to affect the protein: (1) the DNA, (2) the RNA, or (3) the protein itself. Since the proteins that Dr. Aksenova studies are essential, they cannot be deleted at the gene level due to deleterious effects on the nuclear pore complex. Instead, she and her colleagues deplete the proteins conditionally.

Historically, RNA interference (RNAi) has been a popular method to deplete a target protein. RNAi uses double-stranded RNA to target complementary mRNA for degradation. The phenomenon was first described as "co-suppression" in plants. Researchers found that overexpression of an enzyme necessary for deep violet pigment synthesis blocked biosynthesis resulting in white petunias.<sup>2</sup> Later studies clarified the mechanism in *Caenorhabditis elegans* making it a useful method for gene knockdown.<sup>3</sup>

However, RNAi is an imperfect system. It can take time before the effects of RNAi are observed, and knockdown is not always complete. Dr. Aksenova noted that RNAi knockdown needs multiple rounds of cell division over several days to degrade protein. This makes it hard to study nucleoporins since the complexes break down with the nuclear envelope during cell division in mammalian cell lines.

With the development of the  $\underline{A}$ uxin-Induced  $\underline{D}$ egron (AID) system in 2009 and of CRISPR-Cas three years later, <sup>4,5</sup> Dr. Aksenova and her team had the tools necessary to study the basket nucleoporins when they began the project five years ago.

The AID system is much faster and more efficient than RNAi in knocking down protein levels. With the addition of auxin, protein levels are depleted on the scale of hours rather than days. This allows Dr. Aksenova to observe shorter time points and decipher an order of events among nucleoporin interactions. The CRISPR-Cas system makes it possible for the team to insert necessary AID components into cell lines.

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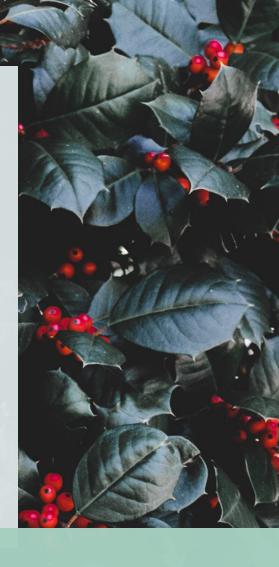
# Then and Now: Studying Essential Proteins of the Nuclear Pore Complex

(continued from page 3)

Even though Dr. Aksenova acknowledged the usefulness of RNAi, she commented that "AID and CRISPR changed [their] lives" to the extent that she "forgot about RNAi after using AID." They were able to knockdown systematically each component of the three subunits of the basket nucleoporin—NUP153, NUP50, and TPR—to determine their distinct roles.

Interestingly, they found that changes in mRNA export upon depletion of TPR were more like changes observed after depletion of mRNA export receptor NXF1, or the GANP subunit of the TREX-2 mRNA export complex, than to loss of the other basket nucleoporins (NUP153 or NUP50).

The application of the AID system and subsequent findings published by Dr. Aksenova and her collaborators could impact how we study different diseases and their mechanisms moving forward. The method pioneered by the team could serve as a template for the systematic study of individual subunits of protein complexes across a wide span of biomedical research.





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- 3. Fire A, Xu S, Montgomery MK, Kostas SA, Driver SE, Mello CC. (1998). "Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans." *Nature* 391(6669):806-811. doi:10.1038/35888.
- 4. Nishimura K, Fukagawa T, Takisawa H, Kakimoto T, Kanemaki M. (2009). "An auxin-based degron system for the rapid depletion of proteins in nonplant cells." *Nat Methods.* 6(12):917-922. doi:10.1038/nmeth.1401.
- 5. Jinek M, Chylinski K, Fonfara I, Hauer M, Doudna JA, Charpentier E. (2012). "A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity." *Science* 337(6096):816-821. doi:10.1126/science.1225829.



# Dr. Erin Walsh Named Acting Director of DIR Office of Education

Congratulations to Dr. Erin Walsh on her appointment as Acting Director of the NICHD Division of Intramural Research (DIR) Office of Education!

Dr. Walsh, former postdoctoral fellow in the laboratory of Dr. Roger Woodgate at NICHD, served as the Associate Director of the DIR Office of Education beginning in 2019 and was promoted to Deputy Director this March.

When Dr. Walsh first joined the DIR Office of Education as a program manager in 2018, she expressed the following: "Regardless of your training level, research and careers in the sciences can be extremely challenging—for me, what is even more rewarding than my own experimental accomplishments, is being able to help young scientists find their way."

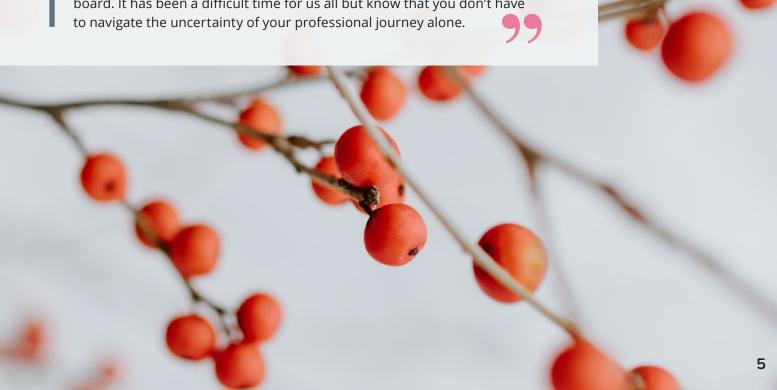
A few more words from Dr. Walsh as she now takes the helm as Acting Director:

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I am very excited for my new role in the office! I have so many great ideas for developing new training programming for the NICHD fellows' community, but I would also love to hear from you all about your ideas and needs as trainees. And although the COVID-19 pandemic prevents us from meeting in-person, as Acting Director, I will maintain an "open-door" policy—always feel free to send me a message (erin.walsh@nih.gov) so we can set up a meeting for discussing your career goals, issues or conflicts you're currently dealing with, application materials, funding opportunities, or even if you just need a sounding board. It has been a difficult time for us all but know that you don't have to navigate the uncertainty of your professional journey alone.



Erin Walsh, PhD







Acting Scientific Director Dr. Mary Dasso as a graduate student in Cambridge, around 1987 (left) and as a postdoc in Kyushu, around 1990 (right).

# NICHD PIs in Training: A Peek into the Past

PHOTOS COURTESY OF EACH INVESTIGATOR.



Dr. Henry Levin as a postdoc at Johns Hopkins Medical School.

"Here's an oldie...this is a photo from 2001 where I was attending the Society for Epidemiologic Research meeting in California along with Subu Subramanian (at Harvard) and Yvonne Michael (at Drexel). I had just finished my PhD!"

—Dr. Stephen Gilman

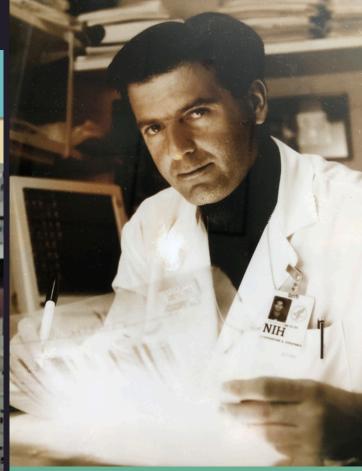


# NICHD PIs in Training: A Peek into the Past

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Dr. Gisela "Gigi" Storz as a graduate student in the 1980s.





Dr. Constantine Stratakis at the time he began his tenure-track position in 1998.

"Here is one from my grad school days (University of Michigan with John Kuwada) at the rig where I spent hours labeling axons in the early brain of zebrafish with Dil or with intracellular injection of Lucifer yellow."

—Dr. Ajay Chitnis



## Scott Morgan's Top Ten Interview Questions Recap

By Leah Meuter

"The oral interview is not the CV, but all the white space in between—the meaningful part," said Scott Morgan, a public speaking coach who has taught science communication for over 25 years. On November 4, 2020, he hosted the workshop "Interviewing for Professional School" for NICHD postbacs.

Mr. Morgan began the workshop by explaining that interview questions historically fall into ten common "buckets," described below. He emphasized that the goal of an interview is not to outguess the interview questions. Instead, be an active listener and identify which bucket the question falls into. By doing so, you have control over the interview and are in a great position to succeed.

#### TEN TYPES OF INTERVIEW QUESTION "BUCKETS"

Mr. Morgan presented the following ten categories of interview questions, with advice about how to answer each type:



#### **Personal Background**

Explain your background up to age 18.



#### **Academic Background**

Talk about your life between the ages of 18 and the present.



#### **Specific Field Motivation**

Discuss why do you want to be a physician or scientist. Be prepared to explain and connect the dots if your path is not linear. Pick one major turning point to illustrate your motivations.



#### 5-Year Plan (or 10-Year Plan)

Show you have thought this career through. Make sure your plan is feasible and genuine. When explaining your future, use "I am" instead of "I hope."



#### **Current Work**

Connect the broad, scientific issue/problem to your research work, creating a common ground with your interviewers. This allows you to explain the relevance of your research to the interviewing school or institution.



#### **Weak Point**

Keep your weakness in the scientific/academic realm if it is appropriate and does not create a red flag. Show the interviewers that you know yourself, and always explain how you are actively working on your weakness.

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#### VIRTUAL INTERVIEW ETIQUETTE

- Use side/front lighting.
- Use a "speaker-phone" voice.
- Have a professional background (avoid using virtual backgrounds).
- Wear bright colors and layered clothing.
- Be enthusiastic.



# Scott Morgan's Top Ten Interview Questions Recap (continued from page 8)



#### **Strong Point**

Focus on technical strengths (for example, you read quickly, know about computer algorithms, or understand western blots). Pick one and illustrate how you use this in your work or everyday life.



#### Why You?

Think about your internal motivation. When you remove time, money, and power, why do you want to go into this career field?



#### Why Them?

Be knowledgeable about the program and funding streams. Make the program feel special and establish a common ground.



#### **Hypothetical Questions (also called Multiple Mini Interviews)**

Remember these questions are hypotheticals ("suppose that" or "what would you do if") that are meant to help interviewers understand your thinking process.

Mr. Morgan highlighted several important interviewing tips throughout the webinar:

- » Pick a single, vivid example and explain why it influenced your career aspirations.
- » Remove self-adjectives (such as ambitious, detail-oriented, hard-working, or motivated) and instead focus on talking about experiences.
- » Formulate single words ("trigger words") that can help you focus your responses.
- » Come prepared with a one-page resume, even during a virtual interview.

Mr. Morgan created a phone app called **3rdi** (available in Spanish, English, and Arabic) to help applicants calm their nerves during interview season. He also recommended we check out the website **www.sciencesketches.org**, which is a website where you can see how scientists frame their research in a larger context.



## Clinical Corner: Meet Dr. Maziar Rahmani

Maziar Rahmani, MD, PhD, DABIM, joined the NIH in 2018 as a clinical fellow in the NIH Inter-Institute Endocrinology

Training Program. He currently studies diabetic vascular disease in Dr. Brant Weinstein's lab at NICHD, exploring whether short-term exposure to hyperglycemia *in vivo* causes long-term epigenetic changes in vasculature.

Dr. Rahmani attended medical school at Babol University School of Medicine in Iran, where he was awarded the Young Investigator Award for founding a lipid research clinic and conducting several randomized clinical trials on high risk populations. After a fellowship from the Research Institute for Endocrine Sciences (RIES) in Iran investigating trends in cardiometabolic diseases, Dr. Rahmani joined the Center for Heart Lung Innovation at the University of British Columbia in Vancouver, Canada as a PhD trainee investigating the molecular mechanism of genes in cardiovascular disease. He continued his vascular research with a postdoctoral fellowship at the Genome Sciences Center (GSC) in Vancouver. Dr. Rahmani completed an internal medicine residency at the

Corner

Maziar Rahmani, MD, PhD, DABIM

George Washington University and is board certified in internal medicine by the American Board of Internal Medicine.

We asked Dr. Rahmani a few questions about his research and interests to get to know the person behind the degree. Introducing Dr. Rahmani:

#### What influenced you to go into endocrinology?

Tragedy can turn everything in life into a painful experience, yet it is from suffering that a phoenix is reborn and rises. I was two years old when my father suffered his first myocardial infarction as a premature complication of his diabetes, and his battle with the condition shaped my childhood. I keenly felt the impact and burden of diabetes on a patient and his family. The process of losing my father was like being reborn; as a gift of that tragic loss, I emerged on the other side as a clinician equipped to treat and fight for other diabetic patients as though they were my own family.

My goal was to practice endocrinology as a clinician scientist, an aspiration that led me to earn a medical degree, a fellowship in the epidemiology of cardio-metabolic diseases, a PhD in molecular/vascular biology, a post-doctoral fellowship in human genetics, an internal medicine specialty training, and now an endocrinology fellowship. The numerous awards of recognition illustrate the breadth of my experience in both clinical and research settings, but the direct impact of my work on the patient is what motivates my professional journey.

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## Clinical Corner: Meet Dr. Maziar Rahmani

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pursue my academic career goals!

What is your most memorable experience so far while at the NIH? It is difficult to pinpoint which memory I am most fond of, as the NIH is a set of institutes unlike any other. The resources available and diverse group of bright minds in attendance means that the opportunities for a clinician scientist are endless. I would consider receiving the email from Dr. Weinstein accepting me to his laboratory as one of my most memorable moments at the NIH. He has provided me a home to grow and

Do you have any hobbies outside of your research and medical work?

When I am not at the NIH, you may find me winding down with music or a good book (political books are the most fascinating to me). As I am originally from Vancouver, Canada, I also enjoy exploring the Washington Metro area with my racing bike. As part of my workout regimen, I have begun boxing, and it has quickly become one of my favorite pastimes. Other than that, visiting my wife, daughter, and mother in Vancouver is high on my priority list when I can get time away from work. We all appreciate trying new restaurants and discussing emerging topics in the world of science. It helps that my wife is also a physician-scientist, and my daughter is currently completing her MPH.



### NICHD DIR & DIPHR Year in Review 2020

#### A look back at Intramural NICHD fellow accomplishments during 2020

The NICHD Division of Intramural Research (DIR) and Division of Intramural Population Health Research (DIPHR) held the first fully VIRTUAL Scientific Retreat on November 13, 2020. The day began with welcoming remarks from NICHD Director Dr. Diana Bianchi, during which she commented on the challenges and opportunities created by the COVID-19 pandemic. The day included 17 short, engaging talks from NICHD scientists at the trainee to principal investigator level and the presentation of the 2020 Mentor of the Year awards (see below). Over 60 virtual posters were available online throughout the following week. A full recap will be available next month!

**Daniel Castranova, MS**, aquatic research specialist in the NICHD Section on Vertebrate Organogenesis, won the **top prize in the 46**<sup>th</sup> **Annual Nikon's Small World Photomicrography Competition** for his photo of the dorsal view of bones, scales, and lymphatic vessels in a juvenile zebrafish. Also named on the award are lab chief **Brant Weinstein, PhD**, and postbaccalaureate fellow **Bakary Samasa**.

**Philip Adams, PhD**, postdoctoral fellow in the lab of **Dr. Gisela "Gigi" Storz**, won an Intramural Research Scholar position this year. In his work, Dr. Adams characterizes RNA-mediated gene regulation in *Borrelia burgdorferi*, the causative agent of Lyme disease, during tick and mammalian infection.

**Mor Alkaslasi**, NICHD Graduate Partnership Program (GPP) student in Dr. Claire Le Pichon's laboratory, received a 2020 NIH Intramural AIDS Research Fellowship award. She uses transcriptomics to study molecular mechanisms of neuronal injury and their roles in neuropathic pain.

Former NICHD fellow **Gülcan Akgül, PhD** (McBain lab), research assistant professor at the University of Connecticut, received a National Alliance for Research on Schizophrenia & Depression (NARSAD) Young Investigator Award from the Brain and Behavior Research Foundation for her proposal on schizophrenia.

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### NICHD DIR & DIPHR Year in Review 2020

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**Brant Weinstein, PhD,** received the NICHD DIR Investigator Mentor of the Year Award.

**Leah Lipsky**, **PhD**, received the NICHD DIPHR Investigator Mentor of the Year Award.

**Hyun Min Jung, PhD,** received the NICHD Fellow Mentor of the Year Award. A mentee of Dr. Brant Weinstein, Dr. Jung has started his own lab as an assistant professor at the University of Illinois at Chicago.

Sincere congratulations to the **18 NICHD fellows** who received a 2021 Fellows Award for Research Excellence, an NIH-wide competition that recognizes the important research of intramural fellows (complete list **here**).

During the 2020 Virtual Postbac Poster Day, a total of **14 NICHD postbacs** received an Outstanding Poster Award for scoring within the top 20% of all posters, NIH-wide. See a complete list **here**.

A big THANK YOU to our 2020 newsletter contributors:

Philip Adams, Mohammad Al-Jundi, Mor Alkaslasi, Aisha Berton, Megan Bohn, Katherine Bonnington, Nickolas Chu, Rachel Dansereau, Mary Dasso, Paul Elizalde, Frances Fernando, Triesta Fowler, Kevin Francis, Stephen Gilman, Iris Hartley, Eric Horstick, Anshika Jain, Crystal Kamilaris, Andy Kouse, Jacob Olondo Kuba, Esther Kwarteng, Henry Levin, Amrita Mandal, Leah Meuter, Yvette Pittman, Maziar Rahmani, Medha Raina, Kyla Roland, Skand Shekhar, Shana Spindler, Gisela Storz, Constantine Stratakis, Nichole Swan, Vivian Szymczuk, Erin Walsh, Lauren Waters, Jeremy Weaver, Sonal Vaid, Ya-Ling Yu, Anna Zenno, and Jessica Zolton.

Please submit your accomplishments for publication in the newsletter throughout the year to <a href="mailto:shana.spindler@nih.gov">shana.spindler@nih.gov</a>.



## **December Announcements**

SEEKING IMAGE SUBMISSIONS FOR THE 16<sup>TH</sup> ANNUAL FELLOWS MEETING

We are beginning our search for the feature image of the 16<sup>th</sup> Annual NICHD Fellows Meeting.

The winning image, chosen by the Fellows Advisory Committee, will be showcased on the fellows retreat website, on posters, and used as the front cover of the event program. Also, to highlight everyone's imagery, all submissions we receive will be used to produce a collage posted on the 2021 retreat website. You can always take a look at the image submissions from previous years at <u>retreat.nichd.nih.gov</u>.

In addition to image resolution and quality, selection criteria include the relevance to our institute's mission and artistic view of the image. All submissions (at the highest possible resolution) should be sent to Nicki Swan (jonasnic@mail.nih.gov) by January 31, 2021, with a brief caption for the image.

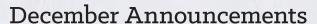
#### INTERESTED IN TAKING AN FAES COURSE FOR YOUR PROFESSIONAL DEVELOPMENT?

The Office of Education will sponsor several NICHD fellows and graduate students to enroll in a career/professional development FAES course for the spring 2021 semester. Course information can be found in the FAES 2020–2021 **course catalog**.

If you are interested, please contact Ms. Carol Carnahan (<u>carnahac@mail.nih.gov</u>) at least four weeks before class begins.

It is important that you discuss this with your mentor and he/she is supportive of your participation.

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SAVE THE DATE: TUESDAY-FRIDAY, JANUARY 26–29
SciPhD Virtual Bootcamp

A training for fellows and graduate students preparing for their professional career transition.

SciPhD will offer a series of four live webinars that cover:

- » Finding jobs
- » Analyzing job ads to determine your skill match and qualifications
- » Developing experience statements and accomplishments that demonstrate your qualifications
- » Generating a draft formatted targeted resume
- » Preparing for the interview process

DAY 1	Tuesday, January 26 9 a.m.–12:30 p.m.	The Business of Science, Dissecting a Job Ad to Identify Critical Skills, Developing a Targeted Resume, Flamingo Software Training
DAY 2	Wednesday, January 27 9 a.m.–1 p.m.	Technical Literacy, Emotional Intelligence, Social Intelligence, Behavioral Interview Exercise
DAY 3	Thursday, January 28 12–4 p.m.	Applied Networking, LinkedIn, Networking Reception
DAY 4	Friday, January 29 9 a.m.–1 p.m.	Project Management, Negotiating Your Departure with Your Pl, Negotiating Salary, Q&A

In addition, each participant will receive their own individual license to the SciPhD online web application Flamingo®, which allows you to put into action the skills you learn in the webinars. Import a job ad, use Flamingo®'s Job Analytics Engine to identify critical skills, and generate a targeted resume.

SciPhD has worked with over 120 institutions over the past 8–10 years on preparing thousands of academic scientists to successfully transition to professional careers.

If you would like to sign up for these live webinar sessions, please contact Ms. Monica Cooper at **cooperm@mail.nih.gov**.

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## **December Announcements**

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### AAAS MASS MEDIA SCIENCE & ENGINEERING SUMMER FELLOWSHIP Applications due January 1!

From the AAAS Mass Media Fellowship website:

"This highly competitive program strengthens the connections between scientists and journalists by placing advanced undergraduate, graduate, and post-graduate level scientists, engineers, and mathematicians at media organizations nationwide. Fellows work as journalists at media organizations such as National Public Radio, Los Angeles Times, WIRED, Milwaukee Journal Sentinel, and NOVA...

...For 10 weeks during the summer, the AAAS Mass Media Science & Engineering Fellows collaborate with media professionals at radio and television stations, newspapers, and magazines. As part of their job, the scientists and their journalist-hosts strive to make science news easy for the public to understand."

For additional information about the program visit **aaas.org/mmfellowship**.

#### GAIN PROGRAMMING SKILLS WHILE TELEWORKING FROM HOME

During this time of extended telework, the NICHD's Bioinformatics and Scientific Programming Core (BSPC) is offering to help fellows gain valuable programming and data analysis skills. BSPC can provide several resources for learning the R programming language as well as develop custom learning plans using online resources to meet specific learning goals. If you are interested in programming and data analysis, please contact Dr. Ryan Dale at <a href="mailto:ryan.dale@nih.gov">ryan.dale@nih.gov</a>.

### **December Events**

WEDNESDAY, DECEMBER 2, 1-2 PM (VIRTUAL)

"Speaking About Science"
Public Speaking Coach, Scott Morgan

As a launching pad for our Annual Postbac Seminar Series, on Wednesday, December 2, Public Speaking Coach Scott Morgan will offer his acclaimed workshop "Speaking About Science." This is a great opportunity for newer postbacs to learn strategies and tips for giving effective science presentations, whether at lab meetings or for larger audiences of broad scientific backgrounds.

"Speaking about Science" is a highly interactive workshop that introduces a nine-step preparation process to prepare a clear and engaging talk for a variety of scientific audiences.

#### Topics include:

- » Presenting data
- » Identifying theme and focus
- » Creating effective visual aids
- » Beginning and ending a talk

Please email Monica Cooper (cooperm@mail.nih.gov) if you plan to attend.

#### THURSDAY, DECEMBER 10, 9:30 AM-4 PM

#### **Ethics in Research Training for Postbacs and Graduate Students**

From the OITE website:

Training in Responsible Conduct of Research is an essential component of your development as a scientist. This course will use lectures, group discussions, and case studies to explore the principles of research ethics. The full-day course is split into a morning and afternoon session (attendance at both is *required* for course credit.) Each class accommodates 70 people. Certificates will be awarded to those that complete the course. Topics to be covered include:

- » Overview of research ethics (current topics and historical studies)
- » Formal research misconduct (falsification, fabrication, and plagiarism)
- » Ethical research involving animal models and human subjects
- » Data management
- » Mentor/mentee relations
- » Conflict of Interest
- » Conflict resolution and reporting
- » Strategies for excelling as a trainee in an ethical manner

This course *must* be completed by all postbacs and graduate students, in the first training year. Follow this link to register: **Ethics in Research Training for Postbacs & Graduate Students**.

#### **ONGOING EVENTS AROUND CAMPUS**

NIH-Wide Office of Intramural Training and Education (OITE) Events

For more information and registration, please visit **Upcoming OITE Events**.

#### **NIH Library Training and Events**

For more information and registration, please visit the NIH Library Calendar.